Alpha-Iduronidase Enzyme Activity in Leukocytes

Disease Overview

Mucopolysaccharidosis type I (MPS I) is a progressive disorder that ranges in severity and can affect numerous systems throughout the body. Subtypes include attenuated MPS I (previously known as Hurler-Scheie and Scheie syndromes) and severe MPS I (formerly Hurler syndrome). Symptoms vary widely but can include cardiomyopathy, "coarse" facial features (eg, thickening of the earlobes, lips, outside of nostrils, and tongue), intellectual disability, organomegaly, and progressive skeletal dysplasia.¹

Genetics

Gene

IDUA

Inheritance

Autosomal recessive

Incidence

MPS I: Approximately 1/70,000

- Attenuated MPS I: 1/500,000¹
- Severe MPS I: 1/100,000¹

Genotype/Phenotype Correlation

<table>
<thead>
<tr>
<th>MPS I Subtype</th>
<th>Characteristics</th>
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<tbody>
<tr>
<td>Attenuated MPS I</td>
<td>Variants are often milder (eg, single base-pair substitutions)</td>
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<td>- Some residual enzyme function is retained</td>
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<tr>
<td>Severe MPS I</td>
<td>Associated with more severe, nonsense variants</td>
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<td>- Profound alpha-iduronidase deficiency</td>
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Test Interpretation

Results

An extremely low or undetectable level of alpha-iduronidase enzyme activity in leukocytes is consistent with MPS I.
Limitations

Testing for alpha-iduronidase enzyme activity:

- Cannot differentiate between attenuated MPS I (ie, Hurler-Scheie and Scheie syndromes) and severe MPS I (Hurler syndrome)
  - Categorization depends on clinical and/or molecular genetic findings
- Cannot predict carrier status for MPS I
- Does not evaluate enzyme deficiencies in other MPS types

Additionally, pseudodeficiency has been demonstrated for this enzyme due to specific gene variants that affect the exogenous substrate but not endogenous substrates. Individuals with pseudodeficiency are not affected with MPS I.

References